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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HUTSON, RICHARD G	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 03/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/282,239	GOLDMAN ET AL.	
	Examiner	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25,26 and 29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25,26 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants amendment the specification and of claims 25, 26 and 29 in the paper of 12/22/2003, is acknowledged. Claims 25, 26 and 29 are at issue and are present for examination.

Applicants' arguments filed on 12/22/2003, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Specification

The disclosure is objected to because of the following informalities:

Previously, it was pointed out to applicants, on page 11, lines 1-17 of the specification applicants follow this definition by list a number of illustrative possible cell and promoter combinations which can be used in the invention including: mature oligodendrocyte and a cyclic nucleotide phosphodiesterase I promoter, a myelinating oligodendrocyte and a myelin basic core promoter, an oligodendrocyte and a JC virus minimal core promoter, a precursor and a JC virus minimal core promoter or an oligodendrocyte precursor and a cyclic nucleotide phosphodiesterase II promoter. This portion of the specification is objected to for the reference to "a precursor and a JC virus minimal core promoter". It is not clear what type of cell a "precursor" refers to.

In response to this, applicants amended the specification from "precursor" to "progenitor", but made no comment beyond the actual amendment. It now remains unclear what type of cell a "progenitor" is.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 25 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 25 is indefinite in that it is confusing in the recitation "...wherein the mitotic oligodendrocyte progenitor cells are derived from a post-natal human..." Specifically applicants intended meaning of the term "derived" in the context of this claim is unclear. It is unclear if it is applicants intent that the referred to oligodendrocyte progenitor cells are "isolated" from a post-natal human or if the oligodendrocyte progenitor cells are isolated from "a cell which is derived" from a post-natal human which would also include cells that were derived from a post-natal human as a result of some modification.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25, 26 and 29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection was stated in the previous office action as it applied to previous claims 25, 26 and 29. In response to this rejection applicants amended claims 25, 26 and 29 and state that applicants traverse the rejection as it applies to the newly amended claims.

Applicants have now amended the claims such that "**a** cyclic nucleotide phosphodiesterase 2 promoter" is transcriptionally active in all of the cells of the enriched preparation. The specification, however, only provides the representative species of enriched or purified preparations of human mitotic oligodendrocyte progenitor cells, wherein the **human** cyclic nucleotide phosphodiesterase II (P/CNP2) promoter functions in all cells of the enriched or purified preparation, encompassed by these claims (see also above 112 2nd paragraph rejection). The specification fails to describe additional preparations of human mitotic oligodendrocyte progenitor cells, wherein a cyclic nucleotide phosphodiesterase 2 promoter in addition to the human cyclic nucleotide phosphodiesterase 2 promoter functions. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms

that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 25, 26 and 29 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Rao et al. (U.S. Patent No. 6,361,996 B1).

For applicants convenience the previous rejection is repeated herein. Rao et al. teach an isolated, pure and homogeneous population of lineage-restricted oligodendrocyte-astrocyte precursor cells which are capable of self-renewal and differentiation into oligodendrocytes and astrocytes and methods of generating, isolating and culturing such oligodendrocyte-astrocyte precursor cells. The specific pure

homogeneous population of cells isolated by Rao et al. is illustrated in Figure 1 (See specifically cell type –14, and the supporting text) and while applicants specifically teach as an example said pure homogeneous preparation of cells as isolated from rat, applicants point out that the invention encompasses all mammalian neuroepithelial stem cells and is not limited to neuroepithelial stem cells from the rat. Mammalian neuroepithelial stem cells can be isolated from human and non-human primates, equines, canines, felines, bovines, porcines, ovines, lagomorphs, and the like. Thus, Rao et al. anticipates a claim to a enriched or purified preparation of human mitotic oligodendrocyte progenitor cells, wherein an oligodendrocyte specific promoter functions in all cells of the enriched or purified preparation.

Claims 25 and 26 which are drawn to the preparation of oligodendrocyte progenitor cells of claim 29 are included in this rejection because these product-by-process like limitations do not change the oligodendrocyte progenitor cells of claim 29. Rao further teach that a better understanding of a number of tumors and other diseases in humans could be facilitated by a better understanding of these cell types and the ability to isolate and grow these mammalian cells in vitro, which allows for the possibility of using such stem cells to treat neurological disorders in mammals, particularly humans. Further, such mammalian neuroepithelial stem cells can be used therapeutically for treatment of certain diseases, e.g. Parkinson's Disease, such as by transplantation of such cells into an afflicted individual. Moreover, such cells can still further be used for the discovery of genes and drugs that are useful for treating certain of these diseases.

One of ordinary skill in the art at the time of filing would have been motivated to use the methods taught by Rao et al. to isolate an enriched or purified preparation of human mitotic oligodendrocyte progenitor cells from humans so that these pure cell preparations could be used to treat neurological disorders in humans, such as. Parkinson's Disease, such as by transplantation of such cells into an afflicted individual. This motivation is suggested by Rao et al. and the reasonable expectation of success comes from the results of Rao et al. who successfully isolated such an enriched or purified preparation of mitotic oligodendrocyte progenitor cells from rat.

The rejection is stated in the previous office action as it applied to previous claims 25, 26 and 29. In response to this rejection applicants have amended claims 25, 26 and 29 and traverse the rejection as it applies to the newly amended claims.

Applicants submit that the Rao discloses multipotential neuroepithelial stem cells and that these cells are characterized as "multipotential intermediate precursor cells restricted to glial lineages" and that since Rao's astrocyte/oligodendrocyte precursor cells are not committed to formation of oligodendrocytes and therefore are in a less differentiated state than the claimed oligodendrocyte progenitor cells, it is apparent that this reference in no way suggests the claimed invention.

Applicants argument is not found persuasive because applicants submission of the differences between the cells taught by Rao and the cells taught in the instant application as isolated from human are acknowledged and understood, however applicant is reminded that applicants invention as disclosed by applicants specification and applicants invention as encompassed by the rejected claims are not necessarily the

same invention and that applicants should direct their arguments to the rejected claims, not applicants specification. As discussed above and previously, applicants claimed invention is anticipated by or, in the alternative, obvious over Rao et al. Applicants appear to be arguing that based on the above using the teachings of Rao one If skill in the art would not have a reasonable expectation of success in achieving the oligodendrocyte progenitor cell preparation as taught by the instant specification because the cells of Rao are in a less differentiated state then that of the instant invention. While this may be true, it remains to be seen that the cell preparation taught by Rao continues to anticipate an enriched or purified preparation of human mitotic oligodendrocyte progenitor cells including those wherein the cells are derived from a post-natal or an adult human, (see above comments to product-by process issues), wherein cyclic nucleotide phosphodiesterase 2 promoter is transcriptionally active in all cells of the enriched or purified preparation. The preparation taught by Rao is such that a cyclic nucleotide phosphodiesterase 2 promoter is inherently transcriptionally active in all cells of the enriched or purified preparation. This is evidenced by the reference Scherer et al. (Neuron Vol 12, pp 1363-1375, June 1994, see applicants IDS) who teach the differential cellular and temporal regulation of the 2',3'-cyclic nucleotide 3'-phosphodiesterase gene (CNP)and teach that the 2',3'-cyclic nucleotide 3'-phosphodiesterase II promoter is transcriptionally active in oligodendrocytes, Schwann cells and many additional tissues and appears before the appearance of mature oligodendrocytes, in oligodendrocyte precursor cells early in brain development (See page1365-1367, Figures 4 and 5 and supporting text).

Applicants further submit that in addition to the above, Rao also worked with cells from rats rather than from humans, as required by the claimed invention and that for the same reasons pointed out in the June 10, 2002 preliminary amendment based on the "First Goldman Declaration" the teachings of Rao are not pertinent to the claimed invention, although it is noted that the referred to declaration was directed to U.S. patent No. 5,276,145 to Bottenstein, applicants representative notes the issues are substantially the same. Applicants continue to point out that there are fundamental differences between the biology of rat and human oligodendrocyte progenitor cells as well as fundamental differences between the lineage restriction and potential of neonatal and adult oligodendrocyte progenitor cells ("Third Goldman Declaration"). Applicants note that these biological differences pointed out above and in the supporting declarations were not recognized by either Rao or Bottenstein. Based on the above applicants submit that rat oligodendrocyte progenitor cells cannot be considered homologous to its human counterparts and methods that are used for the selective extraction of rat oligodendrocyte progenitor cells do not differentiate between oligodendrocyte progenitor cells and mature oligodendrocytes able to reenter the mitotic cycle.

Applicants further submit that rat oligodendrocyte progenitors and oligodendrocytes both express the antigenic marker recognized by monoclonal antibody O4 (Third Goldman Declaration), but applicants note that this marker is not expressed by mitotic (human) oligodendrocyte progenitor cells., thus a method of separation of these two types of cells in human can not be based on the use of O4 selection.

Applicants finally conclude from above and the supporting declarations, that thus the selective propagation of mitotically active oligodendrocyte progenitor cells from neonatal rat brain, as taught by Bottenstein (or Rao) does not predict the successful isolation of mitotic oligodendrocyte progenitor cells from postnatal or adult human brain tissue.

As discussed above, applicants submission of the differences between the cells taught by Rao and the cells taught in the instant application as isolated from human are acknowledged and understood, however, applicant is reminded that applicants invention as disclosed by applicants specification and applicants invention as encompassed by the rejected claims are not necessarily the same invention and that applicants should direct their arguments to the rejected claims, not applicants specification. As discussed above and previously, applicants claimed invention is anticipated by or, in the alternative, obvious over Rao et al. Applicants continue to argue that based on the above using the teachings of Rao one If skill in the art would not have a reasonable expectation of success in achieving the oligodendrocyte progenitor cell preparation as taught by the instant specification because the cells of Rao are in a less differentiated state then that of the instant invention. While this may be true, it remains to be seen that the cell preparation taught by Rao continues to anticipate an enriched or purified preparation of human mitotic oligodendrocyte progenitor cells including those wherein the cells are derived from a post-natal or an adult human, (see above comments to product-by process issues), wherein cyclic nucleotide phosphodiesterase 2 promoter is transcriptionally active in all cells of the enriched or purified preparation. As discussed

above, preparation taught by Rao is such that a cyclic nucleotide phosphodiesterase 2 promoter is transcriptionally active in all cells of the enriched or purified preparation inherently.

Applicants further submit the significance of applicants present invention is apparent by the reference to a number citations to publications in the field of Multiple Sclerosis.

While the reference to these publications are acknowledged and found of interest, the relevance of such publications is unclear with respect to the patentability of the currently pending claims.

Finally applicants submit that nowhere does Rao teach or suggest an enriched or purified preparation of human mitotic oligodendrocyte progenitor cells where a cyclic nucleotide phosphodiesterase 2 promoter functions in all cells of the enriched or purified preparation.

As discussed above, Rao et al. teach an isolated, pure and homogeneous population of lineage-restricted oligodendrocyte-astrocyte precursor cells which are capable of self-renewal and differentiation into oligodendrocytes and astrocytes and based on the above evidence, the cyclic nucleotide phosphodiesterase 2 promoter is inherently transcriptionally active in all cells of the enriched or purified preparation. While applicants specifically teach as an example said pure homogeneous preparation of cells as isolated from rat, applicants point out that the invention encompasses all mammalian neuroepithelial stem cells including those isolated from human and non-human

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (571) 272-0930. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

Rgh
3/15/2004